In re Application of: Mitrani et al
Serial No.: 10/519,838
Filed: December 8, 2005
Office Action Mailing Date: August 10, 2007

Examiner: Kim, Taeyoon
Group Art Unit: 1651
Attorney Docket: 28888

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 174-218 are in this Application. Claims 174-186, 190-206 and 213-218 have been withdrawn from consideration. Claims 187-189 and 207-212 have been rejected under 35 U.S.C. § 103. Claims 187-188 have been amended herewith. Claims 207-212 have been cancelled herewith.

Drawings

The Examiner has objected to Figures 1, 3, 8-13, 18-24 and 26-28 as being of poor quality. Replacement drawing sheets, in compliance with 37 CFR 1.121(d) are provided herewith.

Claim Objections

The Examiner has objected to the term "is" in claim 187 and states that it appears that this term should be "in" instead. Claim 187 has now been amended thereby rendering moot the Examiner's objections in this case.

35 U.S.C. § 112 Rejections

The Examiner has rejected claims 187-189 and 207-212 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Examiners rejections are respectfully traversed. Claims 207-212 have now been cancelled thereby rendering moot the Examiners rejections with respect to these claims. Claims 187-188 have now been amended.

With respect to claim 188, the Examiner states that the term "angiopump" is not clearly defined in the specification. Claim 188 has now been amended to now refer to the type of tissue biopsied thus rendering moot the Examiner's rejection with respect to this claim.

With respect to claim 187, the Examiner states that it is not clear whether the phrase "being operably coupled" in step (b) of this claim claims physical coupling or functional coupling between the cutting chamber and the implanting mechanism.

Claim 187 has now been amended and the phrase "operably coupled" now defines coupling between the scraper (used for tissue biopsy) and the cutting chamber for performing the claimed method.

As is well known in the art, operable coupling defines a functional (operational) relationship between coupled devices. Although physical coupling can be used for operable coupling, such physical coupling is not necessary. As is described in Example 7 of the instant application, the apparatus of the present invention can use a control system to automate the function of the devices and ensure functional coupling therebetween even in the absence of direct physical coupling. Thus, the phrase "operably coupled" in claim 187 refers to the coupling of operation of these devices and particularly to the fact that such devices are arranged to function in coordination which results in transfer of a tissue biopsy produced by the scraper to the cutting chamber for further processing into the claimed micro-organs.

The coupling between these devices is clearly described in now amended step (b) of this claim which states "using said apparatus to obtain said tissue biopsy from a tissue region of the subject thereby generating the plurality of micro-organs". This limitation clearly implies that a tissue biopsy obtained by the scraper will result in generation of micro organs thereby coupling the operation of these devices within the apparatus.

The Examiner further rejects claim 187 as disclosing a limitation pertaining to the implanting mechanism of the apparatus. Claim 187 has now been amended to remove language pertaining to the implanting mechanism.

Claims 207-212 have been cancelled herewith and as such any rejections directed at these claims are now rendered moot with this response.

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35 U.S.C. § 103 Rejections

The Examiner has rejected claims 187-189 and 207-212 under 35 U.S.C. 103(a) as being unpatentable over Mitrani (US 5,888,720).

The Examiners rejections are respectfully traversed. Claims 207-212 have now been cancelled thereby rendering moot the Examiners rejections with respect to these claims. Claims 187-188 have now been amended.

The Examiner states that Mitrani teaches a method of generating micro-organs from skin biopsy by cutting the skin into multiple fragments with a suitable cutting means and then forming micro-organs.

US 5,888,720 teaches a method for forming an in vitro microorgan culture from a variety of tissues including skin. According to this patent the micro-organ culture can be used in various applications including:

> "(a) identification of factors involved in normal homeostasis of tissues and cells;
> (b) the effect on the normal homeostasis of tissues and cells of changes in the environment of the cells including changes in nutrients and the presence of potentially toxic agents;
> (c) the pathway of changes in the tissues and cells that are triggered at the beginning and during pathogenesis or trauma;
> (d) identification of repair mechanism that reverse the adverse effects in an altered environment associated with pathogenesis or trauma;
> (e) developmental regulation of cells that differentiate during the normal homeostasis of the tissue;
> (f) developmental regulation of specialized structures within the tissue such as hair follicles; and
> (g) organ supplementation where pieces of an individual's organ remains but are insufficient for replacing or regenerating damaged tissue such as occurs in patients with chronic skin ulcers which have healing deficiencies caused by inappropriate blood supply, or where the local skin is unable to heal such as in the condition known as type 1 or type 11 diabetes."

Clearly this patent identifies the main use of the micro-organ culture as that of a test culture for screening molecules or as a research tool for identifying/characterizing biological pathways.

Although 5,888,720 also proposes organ supplementation and tissue repair as an application for micro-organs, it does not describe or suggest a functionally integrated apparatus which can be used for a one step tissue harvesting and processing, since such an apparatus is simply not required for micro-organ preparation as taught by this patent.

In fact, the Example describing preparation of micro-organs from epidermis (Example 1) clearly would not motivate one to automate tissue harvesting and preparation since micro-organ preparation as described in this Example (and throughout this patent) would not benefit from such 'automation':

> "Fresh skin was obtained after surgery, cleaned from underlying fat tissue and cut into 0.4 X 5 cm flaps, which are then transversely sectioned, using a tissue chopper or other suitable cutting means into 300 μm sections under sterile conditions so that the final tissue segments had dimensions of 4 mm in width and 0.3 mm in thickness (see FIG. 1). These microorgans were placed in a 24-well microplate in 400 μl of DMEM in the absence of serum under 5% CO2 at 37 C., under constant shaking at 12x rpm for periods of 1 to 8 days. Twenty micro-explants were grown per well." (Emphasis added)

The above described culturing conditions were also used for generating micro-organ cultures from pancreas (Example 4), liver, kidney, duodenum, esophagus and bladder (Example 6).

Thus, US 5,888,720 teaches that tissue is obtained via surgery, while the micro-organs cut from the surgically removed tissue should be cultured under specific culturing conditions which include CO_2 and constant shaking for a period of 1-8 days. Such conditions are suitable for culturing micro-organs to be used in scientific studies and molecule screening as well as other ex-vivo applications which require constant monitoring and analysis of micro-organs and cells contained therein. No other culturing conditions are taught by this application.

The fact that the micro-organ cultures of US 5,888,720 are mainly utilized in ex-vivo applications and the fact that their preparation involves a lengthy culturing step clearly suggests that automated harvesting and preparation would not solve any technical problem and thus would not provide any benefits to US 5,888,720. In fact, an ordinary skilled artisan privileged to the teachings of this patent would most likely be motivated to seek out technologies which address limitations in the culturing and screening steps and not the harvesting and micro-organ processing steps.

The claimed invention is directed at in-vivo uses of fresh micro-organs and thus the aspect of rapid and automated recovery and processing of tissue is critical especially in cases where autologous tissue is utilized for transplantation.

As is clearly set forth in Example 7 of the instant application, an important object of the claimed invention is the automation of tissue harvesting and preparation, since automation, providing rapid and reproducible processing of the biopsies into identical micro-organs is central to micro-organ use in clinical applications, including clinical applications in which immediate transplantation of harvested and processed micro-organs can provide benefits to a subject.

Since automating tissue harvesting and cutting would not solve any technical problems in US 5,888,720, and since 5,888,720 clearly does not teach or suggest uses of micro-organs which would benefit from such automated approaches (e.g. implantation of autologous micro-organs), Applicant strongly believes that US 5,888,720 would not motivate an ordinary skilled artisan to make the present invention as now claimed.

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In view of the above amendments and remarks it is respectfully submitted that claims 187-189 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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Registration No. 40,338

Date: January 9, 2008

Encls:
Petition for Extension (2 Months)
Formal Drawings Transmittal Letter
Formal Drawings Transmittal Letter
Replacement Drawings
Petition for Color with three (3) sets of Drawings